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10/506,749	06/27/2005	Simon Michael Cutting	1307-27	7672

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
05/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,749	CUTTING, SIMON MICHAEL	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,36,37,39-44,47,49,50,52-54,57-59,67-69,75,80 and 81* is/are pending in the application.

4a) Of the above claim(s) *47,49,50,52,53 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,36,37,39-44,54, 57-59,67-69,80 and 81* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/22/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 32, 36-37, 39-44, 47, 49, 50, 52-54, 57-59, 67-69, 75, 80-81 are pending.

1. Non-elected species OppA a vegetative cell protein, and cytoplasmic vegetative cell protein, as well as the method of claim 75 were previously withdrawn from consideration.

Rejections/Objections Withdrawn

2. ***Withdrawn, Claim Rejections - 35 USC § 101*** Claim 32 has been amended to show the hand of man; therefore the claimed invention is directed to statutory subject matter.

3. ***Withdrawn, Specification*** The disclosure objected to because of the following: Applicant has not pointed out where in the Specification support can be found for the Amendments of paragraphs [002], [0010], [0011], [0013], [0015], [0017], [0019], new paragraph inserted between [0028-0029], [0029], [0032-33], new paragraph inserted between [0033-0034], [0035], [0038], [0044-0045], [0052], [0054-0059] has been obviated by replacing the original narrative.

4. Additionally rrnO was not previously defined to encode rRNA; where is the original descriptive support for the amendment of paragraphs [0032 and 0035]?

5. ***Withdrawn, Claim Objections,*** Claims 32, 34-35, 37, 39, 43-44 , 60-61 objected to because of various informalities is herein withdrawn in light of the fact that some claims have been cancelled, other claims amended to obviate the objections, and other claims addressed under new grounds below.

6. ***Withdrawn, Claim Rejections - 35 USC § 112*** Claims 32, 36, 45-46, 47-48, 50-53, 59, 60-61, 65-66 and 71-73 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is herein withdrawn in light of claim amendments, cancellation of claims, or and other claims addressed under new grounds below.

Information Disclosure Statement

7. The information disclosure statement filed January 22, 2008 has been considered.

Response to Arguments

8. Applicant's arguments filed January 22, 2008 have been fully considered but they are not persuasive.

9. Applicant requests examination of all of the species of invention set forth in the claims, and states independent claim 32 recites three species of invention, a signal sequence which is a targeting sequence, a vegetative cell protein and rRNA of rrnO gene which is a targeting

sequence for translation at the cells ribosome and because all three species were in the originally presented claims that all three alternative should be considered.

10. It is the position of the examiner that a Lack of Unity exists within the claimed invention and therefore the restriction set forth previously was proper. No generic claim has been indicated as allowable, therefore rejoinder is not in effect.

11. With respect to claim 32 and all dependent claims, the examiner is reading claim 32 as asserted by Applicant's Representative in the Remarks submitted January 22, 2008, as well as is follows:

- Claim 32 recites terms (i) , (ii) and (iii).
- After (i), no alternative language "or" is recited after the recitation of the "signal sequence" and therefore appears to be required to be linked to the heterologous antigen in all embodiments.
- After (ii) and before (iii), the alternative language "or" is recited, thus setting forth two alternative embodiments.

12. Applicant's Remarks states that claim 32 sets forth 3 embodiments defined by (i), (ii) and (iii). The examiner would like to point out that despite the fact that three phrases are labeled (i), (ii) and (iii), the language of the claims requires the heterologous antigen to be linked to a signal sequence, if this is not intended, the claim should be amended to clearly reflect each alternative. The claims are internally confusing based upon the language recited and the designators not clearly corresponding to Applicant's Remarks that the claim defines three embodiments, and the term ---or---- is not recited at the end of the phrase labeled (i).

Election/Restrictions

Please Note: In light of the fact that vegetative cell proteins include OppA and cytoplasmic vegetative cell proteins which were not previously examined (paragraph (ii) species, claims and amended claims 47, 49, 50, 52, 53 that recite the phrase "vegetative cell protein" are withdrawn from consideration.

13. Newly amended claims 47, 49, 50, 52-53 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The originally examined Bacillus spore comprised a coding sequence of a heterologous antigen linked to a signal sequence, and a heterologous antigen together with a spore comprising rRNA of the rrnO gene (nucleic acid structure). (the signal sequence and the rrnO sequence both being targeting sequences).

14. The other species directed to a vegetative cell protein was directed to a non-elected species (amino acid structure). Based upon the differing structures and biological functions of the species and the first appearing invention not defining a unifying special technical feature, lack of unity of invention existed and restriction/election was proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. The embodiments directed to vegetative cell protein OppA and cytoplasmic vegetative cell protein stand withdrawn from consideration .

15. Accordingly, amended claims 47, 49, 50, 52-53 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. It was noted by the examiner that no single claim recites the elected combination of structures,

specifically a rrnO gene and tetanus toxin fragment C. The claims examined in the First Action on the merits were examined partially in view of the definition provided in paragraph [0035] of the instant Specification. In light of claims 47, 49, 50, 52-53 being directed to and/or amended to recited vegetative cell protein, these claims now read on a non-elected species of invention. The Lack of Unity of Invention is Maintained for reasons of record and responses set forth herein.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Please Note: The prior art rejection is being maintained over a bacillus spore that comprises a heterologous antigen, linked to a signal sequence which was examined in the first action on the merits.

17. The rejection of Claims 32, 36-37, 39-44, 57-59, 67-69, and new claims 80-81 under 35 U.S.C. 102(e) as being anticipated by Goldman et al (US PG-Pub 2002/0150594, filing date December 19, 2001) is traversed on the grounds that:

a. The instant claims only express the heterologous antigen after germination of the spore, and this combination is not disclosed in 2002/0150594.

b. Asserts that 2002/0150594 does the disclose a coding sequence for an heterologous antigen lined to signal sequence such that it is linked to germination and vegetative cell growth.

18. It is the position of the examiner that Goldman et al at paragraphs [0097], [0098] and [0101] disclose expression of the heterologous antigen during the germination process and the coding sequence is a part of a nucleic acid construct that controls the delivery of the heterologous antigen :

"[0097]For example, controlled delivery of polypeptides, peptides, proteins, nucleic acids and other molecules of interest can be achieved by the controlled lysing of a vegetative mother cell containing the spore systems of the present invention. Alternatively, controlled delivery from spore encapsulate systems can be accomplished by allowing spores of a spore system to germinate and produce the molecule(s) of interest (e.g., polypeptide, protein, or peptide) of interest during the germination process, give rise to vegetative cells that produce the molecule(s) of interest, or release such molecules from the core of the spore. In these ways, the spore systems of the present invention provide a means for controlling the delivery of nucleic acids, polypeptides and other molecules of interest to a target site. This control of delivery encompasses the timing and the location of delivery of polypeptides, polynucleotides, nucleic acids, and other molecules of interest. This controlled delivery of such molecules may be useful in many situations and processes where controlled delivery of such molecules is advantageous (e.g., controlled delivery of an immunomodulatory agent, vaccine composition component, or molecule (e.g., protein) used to a "boost" a vaccine's effectiveness. For example, it may be useful to deliver molecules having biocatalytic activities to a biochemical synthesis or degradation reaction in a controlled manner, e.g., in a bioreactor, at a bioremediation site, in a cleaning formulation, etc."

[0098] Spore systems in which polypeptides, proteins, peptides, polynucleotides, and/or nucleic acid molecules of interest are displayed on, stored within, or expressed by the mother cell, the spore, or cells arising from the spore after germination are provided by the present invention. Genes involved in spore synthesis and structure have been identified and cloned, and promoter sequences from such genes have been isolated and characterized. One of skill in the art will appreciate that by selecting among these promoters and regulatory sequences, it is possible to govern the physical location of expression of the polypeptide of interest in the spore or vegetative cell as well as the timing of expression in the life cycle of the spore and/or vegetative cell. "

[0101]... "Similarly, vegetative cells arising from spores may express polypeptides, proteins, or peptides of interest within their cytoplasm and may secrete such molecules. For example, fusion

proteins with vegetative surface proteins may direct expression to the vegetative cell surface; these proteins may then be used for their intended purpose while still attached to the vegetative surface. Alternatively, these proteins may be released from the vegetative surface to perform an application."

Additionally, the signal sequence of the claims is any type of signal sequence that could direct the heterologous antigen to any location in the spore or the vegetative cell as now claimed. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., signal sequence only expressed in the vegetative cell) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The cited paragraphs of Goldman et al refer to the "protein of interest" which are defined to include heterologous antigens that functions as immunogens or vaccines (see [0190]) . While the preferred embodiments are directed to spore coat protein expression of a heterologous antigen, the reference does disclose more than what is described in the examples, to include vegetative cell expression of a heterologous antigen, the expression of which is controlled by a signal sequence. It has long been held that a reference must be evaluated in its entirety, not on the basis of its preferred embodiments or working examples. *In re Mills*, 470 F.2d 649, 651, 176 (USPQ 198 (CCPA 1972).

It was noted by the examiner that the signal sequence of independent claim 32 is not vegetative cell growth specific and could encompass a spore coat protein signal sequence for expression during sporulation; Applicant's traversal is not commensurate in scope with the instantly claimed invention. Applicant's specification describes spore coat proteins/signal

sequences that direct expression of a heterologous antigen to the surface of a spore "cotA"[0061].

The rejection of claims 32, 36-37, 39-44, 57-59, 67-69, 80-81 under 35 U.S.C. 102(e) as being anticipated by Goldman et al (US PG-Pub 2002/0150594, filing date December 19, 2001) is maintained for reasons of record and responses set forth herein.

19. **Instant claim 32, 44, 59, 80-81**: Golden et al teach, describe and show the formulation of compositions that comprise Bacillus spores (see title, [005]), to include spores of Bacillus subtilis, anthracis, coagulans, globigii, stearothermophilus and thuringiensis (see [0102], col. 2, page 11)

wherein the spores comprise one or more ((see [0209]; see page 12, col. 1, paragraph 1 [0104])) genetic constructs (see [0097], [0061]))

under the control of a promoter (see [0106] "the promoters may be native, or analogous or foreign to the plant host or other type of host"; see [0107} "heterologous promoters"; see [0114 "promoter"]); see [0049 "appropriate promoter and gene fusion can be selected to control the position, amount and hence the availability of enzymatic activity or immunomodulatory or antigenic presentation on the spore"])) A sporulation preferred promoter is a promoter capable of initiating transcription upon or during sporulation."), and further comprises a coding sequence for a heterologous antigen (see page 23, [0190]) the sequence encoding tetanus toxin (see page 23, [0190, middle of paragraph and bottom of paragraph "Spore systems comprising antigens or antigenic peptides associated with such diseases or toxins"]) which comprises at least the C-fragment, as tetanus toxin comprises fragments A, B and C; as well as also comprises wherein tetanus toxin is an antigen (see page 23, [0190, middle of paragraph and bottom of paragraph "Spore systems comprising antigens or antigenic peptides associated with such diseases or toxins"]) ; wherein tetanus toxin is an enzyme that is activated upon expression of the nucleic acid and activation of the link between the alpha and beta(comprises Fragment C) subunits and can be used as a pro-drug or painkiller, is a protein, and has been used as a vaccine antigen (see [0190]).

The Goldman et al spores comprises a gene construct that is a chimeric gene (see page 12, [0106 "chimeric gene"; page 11, [0099] "fused in frame with a nucleic acid molecule encoding a polypeptide, protein or peptide or interest, which may further be operatively linked with a nucleic acid molecule encoding "fusion proteins" (see [0101]) expressed in the cytoplasm or may secrete such molecules. (see [0104]) or a part or all of a spore coat gene" .

The coding sequence for the heterologous antigen is linked to a signal sequence (see page 10, [0097, top 1/3 of paragraph "signal sequence that directs secretion of an expressed protein from the host cell"]) or directing expression in one or more specific locations to include:

- [0049 "the gene fusion can be selected to control the position, amount" of the antigenic presentation]); [0069 "expressed in multiple locations on the spores"] [0068 "spore coat"] see page 10 col. 1, [0094 "encapsulated within the spore (e.g. within the outer coat, inner coat and/or cortex and/or in the core"] , thus disclosing local or site specific delivery of the heterologous antigen.

- the cell barrier (see [0014 "bound to , or contained within the spore"]; [0098 "displayed on, stored within, or expressed by the mother cell"].
- (see page 10, [0097, top 1/3 of paragraph "signal sequence that directs secretion of an expressed protein from the host cell"] and

ribosomal RNA (rRNA see [0180]), and nucleic acid sequences that are "upstream from the start of transcription and involved in recognition and binding of RNA polymerase and other proteins to initiate transcription.

Instant claim 36: the mother cells express the gene construct upon germination of the spores (see claim 16, page 46), wherein the vector is introduced into the bacteria (mother cell) and induced to sporulate (see [0101]); [0122].

Instant claim 37, 40-41: wherein the promoter is inducible (see "initiating transcription upon or during sporulation" or constitutive promoter (see [0114]); expressed intermittently in a vegetative cell (see [0098, the timing of expression in the life cycle of the spore" is determined by the promoter])

Instant claim 39: the gene construct has an enhancer element or upstream activator sequence (see page 10, [0097, top 1/3 of paragraph "enhancers"; [0110].

Instant claim 42: wherein the spore germinates in a human or animal body in the intestinal tract " see [0214] Methods for administering spore systems, spore display systems, and spore encapsulate systems of the present invention include those known to those having ordinary skill in the art. Suitable routes of administration or "delivery systems" include parenteral delivery and enteral delivery, such as, for example, **oral**, transdermal, transmucosal, intravenous, subcutaneous, intramuscular, intradermal, intraperitoneal, intracapsular, intraspinal, intrastemal, intrapulmonary, intranasal, vaginal, rectal, intraocular, and intrathecal, buccal (e.g., sublingual), respiratory, topical, **ingestion**, and local delivery, such as by aerosol or transdermally, and the like. Methods for administering proteins, polypeptides, peptides, nucleic acids, and other molecules of interest to mucosal tissue via pulmonary inhalation, nasal, oral, vaginal, and/or rectal delivery are provided. The methods comprise preparing and administering to a subject a composition comprising a spore system of the present invention. Such composition may include a carrier or excipient".

Instant claim 43: elicits an immune response (see at least [0010-0012]).

Instant claim 57: signal sequence (see page 10, [0097, top 1/3 of paragraph "signal sequence that directs secretion of an expressed protein from the host cell"] and [0094 "; local or site specific delivery of such molecules, to "outer coat, inner coat, and/or cortex and/or in the core "of the spore]; [0098 "displayed on, stored within, or expressed by the mother cell"].

Instant claim 59: secretion {see [0097 "directs secretion of an expressed protein from the host cell"…"controlled release" and 101 "may secrete such molecules"] and glycosylation [0134, middle of paragraph]). While Goldman et al does not recite the terms Type I, II or III secretion, the molecular concept of directed release to the surface or surrounding environment is disclosed, which are the functions carried out by the Type secretion systems of the claims..

Instant claim 67: at least two different spores (see claim 111).

Instant claim 68-69: carrier (see claim 39-41).

Goldman et al inherently anticipates the instantly claimed invention as now claimed.

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

2. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

New claim limitations/Newly submitted Amendments to the Specification/New Grounds of Objection/Rejection

Claim Objections

20. Claim 32 is objected to because of the following informalities: Claim 32 recites the term "Bacillus"; this should be ----bacillus---, in light of the definition in the Specification encompassing both Bacillus and Clostridium species, as well as bacillus rod shaped bacteria, . Appropriate correction is required.

21. Claim 32 and all dependent claims under examination are objected to because of the following informalities:

- Claim 32 recites terms (i) , (ii) and (iii).
- After (i), no alternative language "or" is recited and therefore appears to be required to be linked to the heterologous antigen.
- After (ii) and before (iii), the alternative language "or" is recited, thus setting forth two alternative embodiments.
- Applicant's Remarks states that claim 32 sets forth 3 embodiments defined by (i), (ii) and (iii). The examiner would like to point out that despite the fact that three phrases are labeled (i), (ii) and (iii), the language of the claims appear to only define two embodiments, each of which requires the heterologous antigen to be linked to a signal sequence. The

claims are internally confusing based upon the language recited and the designators not clearly corresponding to Applicant's Remarks that state claim 32 defines three embodiments, and the term ---or---- is not recited at the end of the phrase labeled (i). Appropriate correction is required.

Claim Rejections - 35 USC § 112

22. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Amended Claims 43-44 and 59, and new claims 80-81 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are:

24. the specific type enzymes or species of Bacillus spore that will postranslationally process the signal sequence, the type of Bacillus spore that comprises three secretion systems, Type I, II and III for the adaptation/secretion of the heterologous antigen to induce an immune response (claims 43-44).

25. All bacillus spores do not comprise all three types of secretion system; for example a gram positive bacillus spore would not be expected to comprise a flagella type III secretion system, nor a gram negative rod (bacillus) bacteria that is spore forming to comprise all three types of secretion system (see Hueck, Review of gram negative secretion systems, see page 383, Figure 1, Type I, Type II and Type III). What strains of Bacillus have type I, II and III secretion systems since the claimed spores may comprise multiple signal sequences that direct secretion in multiple ways? Finlay et al teach that Type III secretion systems require at least 20 gene products (see page 719, col. 3, p. 2); the claimed spores do not positively recite the presence of

these essential elements that are required gene products (new claim 81) to insure the expressed heterologous antigen would be secreted through this type III system.

26. The critical enzymes or spore type that would carry out the required function of secretion in a type I, II or III secretion systems in a spore forming bacillus bacteria or post-translationally process the signal sequence in the spore forming bacillus bacteria are not positively recited in the claims. Essential elements are missing from the claims. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claims 32, 36, 37, 40-43, 54, 57, 69 are rejected under 35 U.S.C. 102(a) as being anticipated by Casula et al (May 2002, priority for rrnO is not the earliest filed document, different inventive entity) in light of evidence provided by Ogasawara et al (1983).

29. Casula et al disclose the instantly claimed invention directed to a Bacillus spore (see page 2347 "SL6913 spores"), the spore comprising a chimeric gene (se page 2347, col. 2, p. 2) that is a fusion of the rRNA gene rrnO to a heterologous antigen (specifically LacZ). The chimeric gene comprised a strong promoter in light of the fact that upon germination of the spores the chimeric gene was "strongly expressed"(see page 2347, col.2, second paragraph).

30. The signal sequence being apart of the rnnO gene, which would target the antigen for translation in the cytoplasm ribosomes, a specific part of the vegetative cell.

31. The spores were formulated into a composition that comprised a pharmaceutically acceptable carrier, specifically water (see Casula et al, page 2344, col. 2, p. 5 "washed repeatedly with water"), in a volume of 0.2 ml suspensions (see page 2345, col. 1, p. 2).

32. rnnO comprises a promoter, and a leader sequence (also known as a signal sequence) therefore the heterologous antigen is under the control of the rrnO promoter. rrnO comprises two promoters, one inducible and the other being constitutive (in light of evidence provided by Ogasawara (1983, page 6307, Figure 3, and entire article P1 and P2), Casula et al inherently anticipates the instantly claimed invention as now claimed.

The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Conclusion

33. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

34. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Various references are being cited to show secretions systems of bacteria.

35. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/
Examiner, Art Unit 1645
May 19, 2008

/Mark Navarro/
Primary Examiner, Art Unit 1645